REMARKS

Claims 1, 3-4, 6-9, and 11 are pending in the present application.

In the outstanding Official Action, claims 1-9 and 11 were rejected under 35 USC §103(a) as allegedly being unpatentable over FRANCO et al. This rejection is respectfully traversed.

Applicants respectfully submit that FRANCO et al. fail to disclose or suggest the claimed invention. As the Examiner is aware, the claimed invention is directed to a control-release oral pharmaceutical composition containing as an active ingredient 5-amino-salicylic acid.

The composition comprises an inner lipophilic matrix consisting of substances selected from the group consisting of unsaturated and/or hydrogenated fatty acid, salts, esters or amides thereof, fatty acid mono-, di- or triglycerids, waxes, ceramides, and cholesterol derivatives. These substances have melting points below 90°C and the active ingredient is dispersed throughout the lipophilic matrix.

An outer hydrophilic matrix is also present in which the lipophilic matrix is dispersed. The hydrophilic matrix contains compounds selected from the group consisting of polymers or copolymers of acrylic or

methacrylic acid, alkylvinyl polymers, hydroxyalkyl celluloses, carboxyalkyl celluloses, polysaccharides, dextrins, pectins, starches and derivatives, alginic acid, and natural or synthetic gums. The composition may optionally contain excipients and the active ingredient is present in an amount of 80-95% by weight of the total composition.

Applicants respectfully submit that FRANCO et al. do not teach an inner lipophilic matrix or an outer hydrophilic matrix as set forth in the claimed invention.

FRANCO et al. is directed to a composition based on a "reservoir" system. The composition taught by FRANCO et al. is not based on an actual matrix. The active ingredient is confined within a core which acts as a reservoir from which the active ingredient is released via erosion of the outer coating (see FRANCO et al., page 5, lines 25-30; page 13, lines 5-25; and page 14, lines 10-15).

However, the present invention relates to a "multimatrix system" and not to a reservoir system. This means that the active principle is dispersed in a matrix and is not contained in a core. In order to better explain the differences between a "reservoir system" and a "matrix system", applicants have enclosed four publications in

which the characteristics and the differences between the two systems are further explained. The publications are as follows:

1) Jantzen and Robinson, Modern Pharmaceutics, 3rd Edition, pages 582-588;

2) Paul A. Steward, Review of Controlled Release Methods and Devices, pages 4-6;

3) Physical Pharmacy, Drug Release Design, Chapter 19, page 515, 1993; and

4) Il Prodotto Chimico, pages 20-22, Figures 1 and 4, 1985.

Applicants note that the Il Prodotto Chimico paper is in Italian. Thus, applicants have attached an English translation for the more relevant sections (pages 20 and 22) of the publication.

The Examiner's attention is respectfully directed to the Jantzen and Robinson publication. On page 582, the publication states that "Reservoir devices, as the name implies, are characterized by a core of drug, the reservoir surrounded by a polymeric membrane." Jantzen and Robinson go on to teach that this stands in contrast to matrix devices. On page 586, Jantzen and Robinson state that "Matrix devices, as the name implies, consists of drugs dispersed homogeneously throughout a polymer matrix."

Tables 3 and 5 set forth in the publication also describe the characteristics of a reservoir system relative to a matrix system.

As to the Paul A. Steward article, the article states on page 5 that "Monolotic (matrix) devices are devices for controlling the release of drugs. The article states that they are relatively easy to fabricate, compared with reservoir devices, and there is no danger of an accidental high dosage that could result from the rupture of the membrane of a reservoir device. In such a device, the active agent is present in a dispersion within the polymer matrix."

On page 15 of the Physical Pharmacy article, it is stated that "In contrast to a matrix system, a reservoir device consists of a shell-like dosage form with the drug or agent contained within a rate-controlling membrane".

The Il Prodotto Chimico publication further elaborates on the differences between a reservoir and a matrix system.

Thus, it is believed to be apparent that there are distinct differences between a reservoir system and a matrix system.

In imposing and maintaining the rejection, the Official Action also notes that the present specification

discloses the use of surfactants in the claimed composition. The Official Action then contends that the inner lipophilic matrix must also include these substances.

However, applicants again submit that the FRANCO et al. publication fails to disclose a lipophilic matrix or hydrophilic matrix as set forth in amended claim 1. Applicants also traverse the assertion that one of ordinary skill in the art would be able to optimize the FRANCO et al. product to obtain the claimed invention. As the Examiner is aware, a particular parameter must first be recognized as a result-effective variable, i.e., a variable which achieves the recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. *In re Antonie*, 559 F.2d 618, 195 USPQ 6 (CCPA 1977). As FRANCO et al. fail to even mention a matrix composition, applicants respectfully submit that FRANCO et al. do not teach or suggest that the disclosed "reservoir" system is even capable of being optimized in a manner to obtain the claimed invention. As a result, it is believed that FRANCO et al. fail to render obvious the claimed invention.

The outstanding Official Action also contends that the recitation that an "active ingredient is a least partly inglobated" does not limit the claim to an "active

ingredient dispersed in a lipophilic matrix". However, applicants note that FRANCO et al. do not teach a composition wherein "an active ingredient is at least partly inglobated" or "dispersed" in a lipophilic matrix. Nevertheless, in the interest of advancing prosecution, applicants note that claim 1 recites that the active ingredient is dispersed in the lipophilic matrix. It is believed that Franco et al. fail to disclose or suggest the claimed invention.

Thus, while the outstanding Official Action contends that FRANCO et al. is merely "silent" as to the teaching of a matrix system, applicants respectfully submit that it is not just a matter of FRANCO et al. being silent as to a matrix. Rather, applicants believe that FRANCO et al. simply do not teach a matrix system.

In view of the present amendment and the foregoing remarks, therefore, it is believed that the present application is now in condition for allowance, with claims 1, 3, 4, 6-9 and 11, as presented. Allowance and passage to issue on that basis are accordingly respectfully requested.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit

any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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APPENDIX:

The Appendix includes the following items:

- Four publications describing characteristics and differences between "multimatrix system" and "reservoir system":

1) Jantzen and Robinson, Modern Pharmaceutics, 3rd Edition, pages 582-588;

2) Paul A. Steward, Review of Controlled Release Methods and Devices, pages 4-6;

3) Physical Pharmacy, Drug Release Design, Chapter 19, page 515, 1993; and

4) Il Prodotto Chimico, pages 20-22, Figures 1 and 4, 1985.